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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/626,612	07/27/2000	James C. Liao	06497-013001	9658

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EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	15

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/626,612	Liao
Examiner	**Art Unit**
Rebecca Prouty	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 10, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 5, 9, 11-14, 21-25, 28, 29, and 34-51* is/are pending in the application.

4a) Of the above, claim(s) *1, 5, 9, 11-14, 21-23, 25, 28, 29, 34, 35, and 42-4* is/are withdrawn from consideration.

5) ☒ Claim(s) *36-40* is/are allowed.

6) ☒ Claim(s) *24 and 41* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *11*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 2-4, 6-8, 10, 15-20, 26-27, and 30-33 have been canceled. Claims 1, 5, 9, 11-14, 21-25, 28, 29, 34, 35, and newly presented claims 36-51 are still at issue and are present for examination.

Applicants' arguments filed on 4-10-03, paper No. 13, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 1, 5, 9, 11-14, 21-23, 25, 28, 29, 34, 35, and newly presented claims 42-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention (Claims 22 and 23) or species (Claims 1, 5, 9, 11-14, 21, 25, 28, 29, 34, 35, and newly presented claims 42-51), there being no allowable generic or linking claim. Note in Paper No. 9, applicants elected phosphoenolpyruvate synthase (pps) as heterologous polypeptide. Many of the previously examined claims have been amended to recite a nucleic acid sequence encoding a first enzyme "that catalyzes a reaction in a pathway that produces an isoprenoid". All claims so amended have been withdrawn as pps is not an enzyme that catalyzes a reaction in a pathway that produces an isoprenoid. Wang et al. (Reference AI of applicants PTO-1449 of 12/4/00) show in Figure 1 the pathway

for production of isoprenoids. None of the steps of this pathway are catalyzed by pps. In fact pps catalyzes a reaction which is the reverse of one of the steps in the pathway between glucose and pyruvate (one of two glycolytic products which are the original precursors of the isopentenyl diphosphate unit that is the basic building block of all isoprenoids). As such all of Claims 1, 5, 9, 11-14, 21, 25, 28, 29, 34, 35, and 42-51 which recite this language are withdrawn. Claims 24, and 36-41 which read on the elected species are examined herein.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim is directed to kits comprising a genus of *E. coli* cells having a mutation of the glnL histidine protein kinase gene.

The specification does not contain any disclosure of the structure of the mutations in all mutant *E. coli* having a mutation of the glnL histidine protein kinase gene. The genus of *E. coli* recited is a large variable genus with the potentiality of encoding many different proteins with a variety of effects on

the activity of the glnL histidine kinase produced. Kits in which the mutation does not inactivate the kinase would not be useful for producing acetyl phosphate regulation of a gene ligated to the *glnAp2* promoter but might have other diverse uses. Therefore, many functionally unrelated kits are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus (i.e. *E. coli* having the glnL gene deleted and thus no glnL activity) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. It is suggested that the claim be amended to recite "modified by deletion or an inactivating mutation of the *glnL* histidine protein kinase gene"

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the

> prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liao (WO96/08567) in view of Bock et al. (US Patent 5,830,692), McCleary et al. (Reference AK of applicant's PTO-1449), McCleary et al. (Reference AP of applicant's PTO-1449) and Haldiman et al. (Reference AQ of applicant's PTO-1449) or Feng et al. (Reference AL of applicant's PTO-1449). The rejection is explained in the previous Office Action.

Applicants argue that one of skill in the art would not have been motivated to link the production of pps to the production of acetate because acetate was known to be detrimental to the growth oh cells. This is not persuasive because the production of pps in the method of Liao is necessary **only** in the instance that acetate is being produced (i.e., cells in which the carbon flux away from the aromatic pathway is significant) and the expression of pps will eliminate the acetate production. As such any detrimental effect that might have arisen due to acetate production would be eliminated as the pps is produced. Furthermore, linking the two would prevent the expenditure of metabolic energy to overproduce pps in cell situations where

there is no carbon flux away from the aromatic pathway. As such one would have been motivated to modify the vectors of Liao as suggested.

Claims 36-40 are allowed. While as previously explained the prior art clearly suggests linking pps production to the *glnAp2* promoter for aromatic pathway metabolite production, one would not have been motivated to coexpress pps with the lycopene biosynthetic genes of Claim 36 as pps would be expected to divert carbon away from the lycopene biosynthetic pathway precursor pyruvate. Furthermore, while acetate production might similarly be a marker for significant carbon flux beyond the lycopene biosynthetic pathway as it is in Liao, using pps as the enzyme to try and divert this carbon back into the lycopene biosynthetic pathway would not have obvious because the skilled artisan would expect it to produce an imbalance between the two necessary glycolytic precursors (pyruvate and G3P).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is

not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652